

[0012] FIG. 4 shows the effects of different doses of 2-fluorofucose, administered via drinking water, on antibody core fucosylation. The dot blots show protein loading levels (left) and fucose specific bioluminescence (middle) for untreated control and 1, 10, and 100 mM SGD-2083 (as indicated). The % fucosylation compared to untreated is shown in the graph on the right.

[0013] FIG. 5 shows the effects of administration of 2-fluorofucose on circulating white blood cells and neutrophils. Panel A. Blood samples were collected from individual mice, and the white cell count was determined by counting on a hemacytometer using Turk's solution of exclude red blood cells. Panel B. To determine neutrophil counts, the percentage of white blood cells that were Gr-1+ was determined by flow cytometry and applied to the total cell count determined in (A). Panel C. A pool of lymph nodes was collected from individual mice, single cell suspensions were prepared and cells were counted on a hemacytometer. Symbols represent individual mice (n=3 per group; diamonds, untreated; squares, 1 mM 2-fluorofucose (SGD-2083); triangles, 10 mM 2-fluorofucose; circles, 100 mM 2-fluorofucose).

[0014] FIG. 6 shows the effects of administration of 2-fluorofucose on E-selectin binding to neutrophils. Panel A. An example of neutrophil identification by flow cytometry. Cells were gated on forward and side scatter to include live white blood cells and then applied to the histogram depicting Gr-1 staining to identify neutrophils. The positive cells were gated, the percentage positive cells determined (used for cell counts in FIG. 5B), and the gate was applied to the histograms in (B). Panel B. Examples of E-selectin binding to neutrophils from an untreated animal (left) and an animal treated with orally administered 2-fluorofucose (SGD-2083) at 100 mM (right). Grey histograms show E-selectin binding and the dotted lines show binding of the secondary reagent alone. The geometric mean fluorescent intensity was determined for E-selectin binding. Panel C. Geometric mean fluorescent intensity of E-selectin binding was determined for each animal as in (B) and compared between groups (n=3, per group; error bars represent standard deviation).

[0015] FIG. 7 shows the effects on protein fucosylation for cell lines cultured with certain fucose analogs. The LS174T, PC-3, Ramos, HL-60cy and Caki-1 cell lines were examined.

[0016] FIG. 8 shows the effects of administration of fucose analogs to mouse xenograft cancer models. The results of mouse xenograft models with LS 174T, PC-3, Ramos, HL-60 and Caki-1 cell lines (pre-treated with 2-fluorofucose (SGD-2083)), are shown in panels A-E, respectively. The results of a mouse xenograft model with an untreated LS174T cell lines are shown in panel F.

[0017] FIG. 9 shows the study design (panel A) and results (panel B) of a tumor vaccine model based on preimmunization with killed A20 murine lymphoma cells, followed by challenge with live A20 cells with or without administration of a fucose analog, (2-fluorofucose).

globulin family, or fragments thereof, that contain an antigen binding site(s) that immunospecifically binds to a specific antigen and have an Fc domain comprising a complex N-glycoside-linked sugar chain(s), or (b) conservatively substituted derivatives of such immunoglobulin polypeptides or fragments that immunospecifically bind to the antigen. Antibodies are generally described in, for example, Harlow & Lane, *Antibodies: A Laboratory Manual* (Cold Spring Harbor Laboratory Press, 1988).

[0019] An “antibody derivative” means an antibody, as defined above (including an antibody fragment), or Fc domain or region of an antibody comprising a complex N-glycoside linked sugar chain, that is modified by covalent attachment of a heterologous molecule such as, e.g., by attachment of a heterologous polypeptide (e.g., a ligand binding domain of heterologous protein), or by glycosylation (other than core fucosylation), deglycosylation (other than non-core fucosylation), acetylation, phosphorylation or other modification not normally associated with the antibody or Fc domain or region.

[0020] The term “monoclonal antibody” refers to an antibody that is derived from a single cell clone, including any eukaryotic or prokaryotic cell clone, or a phage clone, and not the method by which it is produced. Thus, the term “monoclonal antibody” is not limited to antibodies produced through hybridoma technology.

[0021] The term “Fc region” refers to the constant region of an antibody, e.g., a C_H1 -hinge- C_H2 - C_H3 domain, optionally having a C_H4 domain, or a conservatively substituted derivative of such an Fc region.

[0022] The term “Fc domain” refers to the constant region domain of an antibody, e.g., a C_H1 , hinge, C_H2 , C_H3 or C_H4 domain, or a conservatively substituted derivative of such an Fc domain.

[0023] An “antigen” is a molecule to which an antibody or antibody derivative specifically binds.

[0024] The terms “specific binding” and “specifically binds” mean that the antibody or antibody derivative will bind, in a highly selective manner, with its corresponding target antigen and not with the multitude of other antigens. Typically, the antibody or antibody derivative binds with an affinity of at least about 1×10^{-7} M, and preferably 10^{-8} M to 10^{-9} M, 10^{-10} M, 10^{-11} M, or 10^{-12} M and binds to the predetermined antigen with an affinity that is at least two-fold greater than its affinity for binding to a non-specific antigen (e.g., BSA, casein) other than the predetermined antigen or a closely-related antigen.

[0025] The terms “inhibit” or “inhibition of” means to reduce by a measurable amount, or to prevent entirely.

[0026] As used herein, “alkynyl fucose peracetate” refers to any or all forms of alkynyl fucose (5-ethynylarabinose) with acetate groups on positions R¹⁻⁴ (see formula I and II, infra), including 6-ethynyl-tetrahydro-2H-pyran-2,3,4,5-tetra-yl tetraacetate, including the (2S,3S,4R,5R,6S) and (2R,3S,4R,5R,6S) isomers, and 5-((S)-1-hydroxyprop-2-ynyl)-tetrahydrofuran-2,3,4-triyl tetraacetate, including the (2S,3S,4R,5R) and (2R,3S,4R,5R) isomers, and the aldose form, unless otherwise indicated by context. The terms “alkynyl fucose triacetate”, “alkynyl fucose diacetate” and “alkynyl fucose monoacetate” refer to the indicated tri-, di- and mono-acetate forms of alkynyl fucose, respectively.

[0027] Unless otherwise indicated by context, the term “alkyl” refers to an unsubstituted saturated straight or branched hydrocarbon having from 1 to 20 carbon atoms

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0018] The term “antibody” refers to (a) immunoglobulin polypeptides and immunologically active portions of immunoglobulin polypeptides, i.e., polypeptides of the immuno-